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FINAL REPORT

1. EUBS2016 Annual Meeting Scientific Activity Report

- a. The Annual EUBS Meeting 2016 was held in Geneva, Switzerland, from September 13-16, 2016. EUBS Meetings provide both an opportunity for young researchers to present their work, as well as a forum for discussion, expansion of research projects, consolidation and initiation of collaborative science projects.
- b. The scientific program consists of a limited number of keynote lectures, free presentations, workshops and presentation of posters. By its very nature, EUBS encourages presentations in the field of hyperbaric medicine, diving medicine and high-pressure physiology. This reflects in the content of the scientific program (see attached PDF). As every year, sufficient discussion time and opportunities for informal contacts and formal meetings is provided. A major role of EUBS is to increase knowledge and foster collaborations in the field of diving medicine and hyperbaric medicine. Its Annual Meeting is the prime (in fact, only) occasion for researchers and clinicians from all European countries to meet in one place, in a relaxed atmosphere, and to exchange views and ideas.
- c. Concurrently, associated and affiliated organizations have had their formal or informal meetings during the days of the EUBS Meeting.
 - i. Diving and Hyperbaric Medicine (DHM) journal – (Informal) Editorial Board meeting
 - ii. European Diving Technology Committee (EDTC) – Medical Panel meeting
 - iii. European Committee for Hyperbaric Medicine (ECHM) – Board of Representatives and Executive Board meeting
 - iv. European Baromedical Association for Hyperbaric Nurses and Technicians (EBAss) – Executive Board meeting
- d. The EUBS has its face-to-face Executive Committee meeting and Annual General Assembly. As a result of discussions prior to and during the meeting a number of important developments were noted and decisions taken accordingly:
 - i. Adaptation of EUBS membership plans, offering the possibility to subscribe to the DHM Journal without being a full EUBS member. The aim of this is to increase the distribution of DHM, making it easier to reference from and more attractive to new submissions.
 - ii. Initiation and follow-up reports of EUBS Committees supplementary to the existing Liaison Committee:
 - “Research Education Committee”, tasked with preparing educational activities and scientific guidance procedures in relation to diving medicine research

- education. The tasks of this Committee were expanded to encompass also the selection and attribution of research and travel grants to young researchers
- “Journal Governance Committee” tasked with managing all tasks and procedures other than purely editorial in relation to the “Diving and Hyperbaric Medicine Journal” – this Committee is composed of two members from EUBS and two of SPUMS (both Societies being co-owners of the journal)
 - “Publications Committee” tasked with selecting and compiling endorsements and guideline texts for publication on the EUBS Website, with the explicit aim to make EUBS more “visible” to the diving and hyperbaric medical communities as a reference organization
- iii. Signing/renewal of Affiliate Agreements with UHMS, SIMSI, BVOOG-SBMHS, SHF and GTUEM allowing reduced membership fees for these Societies’ members
- e. The 2016 EUBS Conference opened, on Sept 13, 2016, with a Special Session on research techniques – specifically oriented toward “the young investigator”. EUBS has in the previous years, progressively worked to establish a “Research Education Committee” within its Executive Committee. This Committee served as faculty for the above mentioned pre-course. Topics included the relevance of rat (and other animal) models in the assessment of decompression sickness treatments (S. de Maistre, Toulon, France); the logistic, ethical and scientific difficulties in organizing a true “RCT” type research project with hyperbaric oxygen therapy in humans (B. Degraz, Geneva, Switzerland), discussing, among others, the pharmacological effects of slight to moderate hyperoxygenation (such as in the use of hyperbaric air in the control arm of a comparative study. S.L. Blogg, the European Editor of DHM (Diving and Hyperbaric Medicine Journal), provided an introduction on the importance of proper scientific writing. C. Balestra gave an overview of currently available granting possibilities, with an emphasis on the procedures and selection processes in the European Commission Framework Programmes.
- f. In recent years, the use of hyperbaric oxygen in the treatment of cerebral infections and traumatic brain injury has been intensively investigated; this interest was reflected in a first scientific session: “HBO and neuroscience”.
- i. Hadanny et al. (Tel Aviv, Israel) showed F-MRI results, coupled with cognitive function measurements (Neurotrax software) in chronic TBI patients (mean time before treatment 6.7 years) after a 60 treatment (3 months) HBO treatment (2.0 ATA, 90 minutes, 5x/week). Signs of increased microvasculature and improvement in functional function of the long axonal tracks (cingular, corpus callosum), as measured by Diffusion Tension Imaging (DTI), were presented. The improvement in cognitive function was in the order of 15-20%. There was however no control group and the group comprised only 15 patients (these were a majority of Motor Vehicle Accidents victims). DTI as well as Neurotrax do however seem to provide an objective measure of higher brain function, and may well be considered for systematic inclusion in future studies.
 - ii. F. Lind (Stockholm, Sweden) pleaded for the creation of a European registry for the treatment of CNS infections with HBO. Two types of infections can be treated with HBO: acute life threatening infections and chronic refractory infections (Staphylococcus Aureus, Pseudomonas Aeruginosa – biofilm impedes oxygen diffusion and thus antibiotic efficacy). Preliminary results of HBO treatment for infected neurosurgically implanted devices are promising (paper in preparation). As these and e.g. intracranial abscesses are rare and there are no large randomized clinical trials available, only retrospective data and “common sense” can currently be considered. A recently published trial showed a much higher resolution rate in those patients treated with HBOT (2/14 recurrence, as opposed to 15/26 in the control group; and statistically significant better outcome scales)
 - iii. Hadanny et al. (Tel Aviv, Israel) examined the prognostic indicators in a retrospective review of Central Retinal Artery Occlusion patients treated with HBO therapy, less than

20 hours after the start of symptoms. His study group was carefully examined to excluded those with a patent cilioretinal artery (known to be spontaneously improving over a short time due to blood flow redistribution). Measure of effect was the Best Visual Acuity pre- and post-treatment.

128 patients (out of a total of 225 patients treated in a time span of 16 years) fulfilled the inclusion criteria. Of those, 67.2% showed clinical improvement; 25% was discharged with a visual acuity of >1 LogMAR (not clinically blind). Analysis of prognostic factors showed that the proportion of patients with clinically meaningful visual improvement was significantly higher in patients without Cherry-Red Spots (CRS) compared to patients with CRS at presentation (86.0% vs 57.6%, $p<0.0001$)

The percentage of patients with final BCVA better than 1.0logMAR was also significantly higher in patients without CRS than patients with CRS at presentation (61.0% vs 7.1%, $p<0.0001$). There was no significant difference in the time delay to treatment in the two subgroups ($p=0.06$). It was concluded that ocular fundus findings (notable the presence of CRS), rather than the time delay from symptoms onset, can be used as a predictor of HBOT success.

- iv. Treating intensive care (including brain-injured) patients in the acute phase of their illness necessarily involves intubated/ventilated HBO treatments. The strategy of systematically performing myringotomies (tympanic membrane perforations) in these patients has long been recommended as it will prevent middle ear barotrauma (MEBT) in these patients, who are unable to perform middle ear equalization maneuvers. However, time constraints and the necessity to have an ENT specialist on call or on-site to perform this procedure, often preclude this in an emergency setting. No systematic research has been done as of today whether not performing tympanotomies significantly increases the risk of serious MEBT. A call for participation in a multi-centric clinical prospective trial was launched by P. Bothma from the London Whipps Cross and Gorleston Hospitals in the UK. Meanwhile, Lafère et al. (Brest, France), presented their results from middle ear pressure measurements in deeply anesthetized OR patients, at baseline, after induction with opioids/propofol and after administration of neuromuscular blockade (NMB). No significant pressure or volume changes of the middle ear were observed, however, there was a significant increase in compliance after the combined injection of opioids and hypnotic agents ($24\pm 7.13\%$, $p=0.001$). Injection of NMB agents did not further improve compliance ($23\pm 8.9\%$, $p=0.011$).

g. The second scientific session focused on diving-related respiratory aspects.

- i. Yu et al. (Shanghai, China) presented experimental results on pulmonary endothelial cells (PMVECs), showing that Endothelial Microparticle (MEP) release from these cells after contact with nitrogen bubbles, have profound and prolonged effects on endothelial permeability, pro-inflammatory cytokine expression and increased intracellular ROS (Radical Oxygen Species). These effects could be significantly reduced by lysing EMPs with surfactant FSN-100.
- ii. Vandenhoven et al. (Brussels, Belgium) studied the respiratory physiology of novice breath-hold divers (BHD) in a recreational diving setting. It was shown that BHD were able to increase their Maximal Voluntary Ventilation after a relatively short BHD training program, indicating that BHD might also be useful for training respiratory muscle strength and coordination in selected patient populations as part of a physical rehabilitation program.
- iii. Castagna et al., from the French Navy Research Institute (ERRSO) in Toulon, France, studied the effects of the negative pressure breathing imposed by negative Static Lung Load (SLL) in divers wearing a Back Mounted Counterlung Rebreather, exploring the hypothesis that this would lead to an increase of extravascular lung water. They subjected 16 divers to two 30-minutes shallow dives, one in Prone-Static position with compressed air (PS, SLL >0) and the second supine finning (Negative Exercise NE, SLL <0). They showed that NE imposed 4 times higher minute ventilation and an 80-fold higher Inspiratory Work than PS; the cumulative Work of Breathing (WOB) during NE amounted

to 130 times that during PS. Ultrasound Lung Comets (ULC) indicative of extravascular lung water accumulation, were detected after NE but not after PS. Right-sided cardiac echographic parameters were all markedly changed after NE, even though left ventricular volume and ejection fraction were constant. They concluded that NE seems to impose a significantly higher right heart preload, poorly compensated by a proportional increase on the left cardiac output. This creates conditions that are favorable for occurrence of Immersion Pulmonary Edema.

- iv. Schellart and Sterk (Amsterdam, The Netherlands) reported on the influence of the wet diving suit on standard spirometry values, indicating that, notwithstanding the many possible confounding factors such as diving suit thickness and fit, a change in Forced Vital Capacity in the order of -4% may be expected.
- h. A Special Session, named "Hypo-hyperbaric paradox" explored effects of (adaptation to) hypoxia, both in freediving and high altitude exploration, as well as the therapeutic use of hyperbaric oxygenation in frostbite. It seems possible that the therapeutic window in cases of frostbite may be extended to several days, however, conducting randomized controlled studies is virtually impossible. A registry has been set up, the IFR (International Frostbite Registry) which hopes to collect initial and follow-up data on a maximum number of cases.
- i. The second day of the meeting started off with a session on Hyperbaric Oxygenation and included biochemical studies as well as clinical reports.
 - i. Normobaric 100% oxygen administration was explored by a Norwegian group for its effects on Nitric Oxide (NO) synthesis. In contrast to previous published reports, Hesthammer et al (Bergen, Norway) found that the decrease of tetrahydrobiopterin and concomitant reduction of phenylalanine conversion, possibly impairing the de novo synthesis of NO, was completely reversed after 60 minutes. It seems that the decrease in NO-generation is only transient and returns to base levels within an hour. Diving with increased pO₂ levels should therefore not be seen as increasing the risk for decompression sickness in comparison to air diving.
 - ii. Klapa et al. from the German Naval Medical Institute (Kronshagen, Germany) explored the effects of an acute hyperoxic exposure on the T and B Cells immunologic response. A 30 minute hyperoxia provoked in the peripheral blood mononuclear cells (PBMC) a marked increase of the "central memory" and "effector" T Cells, which expressed a TH1 phenotype. The levels of regulatory T Cells did not change, however an increase in regulatory B Cell shifted the Treg/Breg balance. This partially confirms previous animal studies.
 - iii. A Swiss group led by D. Levigne (from the Division of Plastic Surgery of the University of Geneva) performed an animal study on wound closure, perfusion and contraction in 4 different conditions of ischemia and (hyper)glycaemia, to investigate the effect of Hyperbaric Oxygenation Therapy (HBOT) in chronic diabetic wounds. HBOT increased blood flow and accelerated wound closure in ischemic and hyperglycemic wounds, most significantly when the two conditions were combined. Wound contraction and re-epithelialization were equally stimulated by HBOT. However, the acceleration of wound contraction was not associated with increased myofibroblasts expression. When ischemia and hyperglycemia are combined, as it is often the case in diabetic patients, the effects of HBOT are most significant.
 - iv. Estimating the cost impact of adding HBOT to the treatment of a chronic diabetic foot ulcer (DFU) is difficult if not impossible to perform. Longobardi et al. (Ravenna, Italy), based on a Europe-wide survey, calculated the costs of treatment of DFU as well as the cost associated with above the knee amputation (AKA). Using the comparison between the county of Romagna in Italy (where HBOT is routinely used for DFU treatment) with the Emilia Romagna region (where HBOT is not routinely used) they showed a 5-fold reduction in AKA in the HBOT group (0.18/1000 AKA in Romagna vs 0.67-0.75/1000 AKA in Emilia Romagna – USA data from 2010 indicate a 0.4/1000 AKA rate there). Using this Number Needed to Treat (NNT) of 4 (with 35 HBOT sessions as a guide) and the average

costs for DFU treatment and AKA obtained from 27 European countries, they calculated an indicative annual cost savings of 283,500 – 396,900 Euros, furthermore excluding indirect social costs of rehabilitation for AKA.

- v. Another controversial indication for HBOT, Femoral Head Necrosis, was subjected to a retrospective review by G. Bosco and E. Camporesi (Padova University, Italy and Tampa, FL). Reviewing 249 cases treated from 2004 to 2013, they concluded in a high efficacy of HBOT both in Visual Analogue Scoring (VAS) and MRI analysis (improvement of 90.9% in Ficat Stage I, 82.1% in Ficat Stage II and 9.3% in Ficat Stage III). Joint survival at a mean follow up of 6 years+/- 3 was 98.1%, 91.3% and 49.2% respectively for Ficat Stage I, II and III.
 - vi. Brauzzi et al. (Rome, Italy) surveyed the incidence of decompression sickness in hyperbaric chamber inside attendants, and reported that that with (Italian) current HBOT protocols and practice, the risk appears to be extremely low. Only three cases have been published over the past 30 years, of which one was only a suspicion, and another one was due to an accumulation of risk factors and deviation from the recommended protocol. They conclude that screening chamber attendants for Patent Foramen Ovale (known to increase the statistical risk for DCS by a factor of 3-5), is not warranted in view of the low risk and high cost.
- j. This session was followed by a second session on diving decompression.
- i. Lu Shi et al. (Shanghai, China) reported on their calculations of high-altitude diving decompression tables using helium-oxygen mixtures. Using standard conversion of air pressure ratios at sea level vs. altitude, 45m/30min, 55m/30min, 65m/30min, and 75m/20min of helium-oxygen conventional diving was performed above 3300m sea level in Tibet. Bubble sounds in the precordial region were monitored at 6m, 4m, 3m, 2m and 0m stops with Doppler ultrasound monitor among all 28 person-times diving decompression. No Venous Gas Emboli (VGE) sounds were detected, and no decompression sickness resulted. It was concluded that, in this limited group of 8 divers, the calculated dive profiles were safe. This study adds to the current limited data available for high-altitude decompression diving, although of course it is a limited series of dives in a (probably) highly selected diver population.
 - ii. A Greek group (Evgenidis et al., Thessaloniki) proposed a novel way of measuring decompression stress, by using electrical impedance spectroscopy measurements. By means of a linear statistical analysis of the Low (0-0.5 Hz) and Medium Spectrum (0.5–10 Hz) frequencies, the effects of VGE could be demonstrated in a series of test dives in the Nemo33 swimming pool in Brussels, Belgium (33mfw for 20 minutes). There appears to be a fair agreement between the (patented) i-VED ("In-Vivo Embolic Detector") and the ultrasound measurements, which makes this technique potentially useful for early and continuous bubble detection.
 - iii. Meanwhile, JP Imbert et al. reported on the measurement of decompression stress and oxidative stress in saturation off-shore divers (Technip, France) using echocardiography and precordial Doppler for VGE and Flow-Mediated Dilation (FMD) as a measure of oxidative stress. The saturation profiles did not produce any VGE during the entire 12 hours monitoring period, leading the authors to suggest that the 24 jour post-dive observation period can probably safely be shortened. However, FMD values did not return to baseline before 12hours, and oxidative stress associated to endothelial function variation remained significant, despite the moderate chamber oxygen levels (480-500 mbar to 13m, 22% to surface). This suggests that bubble grade is mainly affected by the physics of gas exchange and bubble growth but that FMD is mainly associated to oxidative stress. These two measures define two independent dimensions of decompression stress. Their interaction suggests that a safe decompression is a trade-off between oxygen levels and bubble grades.

- k. D. Mathieu (Lille, France), chairman of the European Committee for Hyperbaric Medicine (ECHM), reported on the conclusions of the 10th European Consensus Conference on Hyperbaric Medicine which took place on April 14 and 15, 2016. Apart from the division in Type 1 (strongly indicated), Type 2 (suggested) and Type 3 (optional), a new category of "Negative Recommendations" was created, with a "Type 1 recommendation for NOT using HBOT". Indications currently in this category are

- i. Autism spectrum disorders
- ii. Cerebral palsy
- iii. Multiple sclerosis
- iv. Placental insufficiency
- v. Stroke, acute phase
- vi. Tinnitus

An Executive Summary Report of this Consensus Conference has been published in *Diving and Hyperbaric Medicine* 46(2), June 2016, and the full report is in preparation.

- l. Two final sessions of this conference day were devoted to case reports in HBOT and diving medicine, with
- i. two papers (Schipke, Varlet) discussing the forensic examination of deceased divers;
 - ii. an Israeli paper (Y. Arieli) preliminarily reporting a possible dose-dependent disruption of the Blood-Brain Barrier resulting in oxygen toxicity convulsions (Sprague-Dawley rats, 6 ATA)
 - iii. an interesting clinical application of immersion-induced fluid shift, capable of preventing hemodialysis-induced intravascular hypovolemic symptoms after extraction of three liters of body water – simply by placing the patient (during the hemodialysis session) in a head-out immersed position in thermoneutral water (Doenyas-Barak et al., Tel Aviv, Israel).
 - iv. a report from the Environmental Lab of the Brest University, France (Lautridou et al.) showing that by selective breeding of Wistar rats is capable of inducing decompression sickness resistance in only three generations (initial incidence of DCS 66%, incidence in the third generation 33%). This research group will increase research into the genetic and physiological comparisons between the initial Wistar rat strains and the new, resistant, population.
 - v. A report from the Shanghai Faculty of Naval Medicine (Zhang et al) on the apparent protective effect of Aescin (Horse Chestnut extract, commonly used to treat and prevent venous insufficiency) on the incidence and mortality of DCS in a severe rat decompression model (7 ATA 90 minutes, lineal decompression to surface pressure in 3 minutes). Both incidence and mortality decreased significantly after a 7 day supplementation with Aescin ($p=0.001$ and $p=0.0045$ respectively) and latency to DCS and survival time likewise increased. Aescin appeared to decrease changes in endothelial indices, oxidative response and inflammatory reactions induced by DCS. The authors hypothesize that Aescin (due to its endothelial protective, anti-inflammatory and anti-oxidative properties) may be used as a prophylactic drug for DCS, owing to its low risk of side effects.
- m. There were 27 posters on HBO Therapy and 17 posters on Diving Medicine. HBO Therapy posters were mainly devoted to case series and retrospective reviews.
- In the Diving Medicine posters a number were dealing with breathing gas issues.
- i. Luddecke et al. (P-06) assessed changes in pulmonary and cardio-pulmonary parameters before start of oxygen-diving training and during active duty in 221 male oxygen-divers, up to 13 years after their initial examination. In contrast to previous studies there were significant changes in the Resistance (Reff), forced expiratory flow at 50% and 25% and the time course of the diffusion capacity, indicating oxygen mediated long-term effects.
 - ii. Markus (P-12) analyzed the redox state of professional SCUBA (police) divers during one of their training periods. It was shown that although values of nitrites (NO₂⁻) were significantly increased after a single dive on Day 3 of their training period (30 msw, 30

- minutes), other reactive oxygen species (ROS) indicators (O₂⁻, H₂O₂, TBARS, Catalase, Superoxide Dismutase) were unchanged. This may indicate an upregulation/adjustment of the anti-oxidant defenses in these (already) frequent diving population.
- iii. Tillmans (P-27, Zetterstrom Award winner) examined the lymphocyte population changes after hyperoxic exposures; it was shown that after a single hyperbaric oxygen exposure (2.8 ATA 30 minutes), a 2.9 fold increase in DNA strand breaks was observed in healthy male applicant-divers. A significant increase of the T-cell lymphocyte population was found without concomitant increase in B-cells. No relevant changes in apoptosis induction in either population was found. Possible explanations may reside in either a resting (non-proliferating) state of Peripheral Blood Mononuclear Cells (PBMC) or an early DNA-repair process in these cells.
 - iv. Schellart (P-34) proposed correction factors for the adiabatic processes in instantaneous gas consumption calculations.
- n. Other posters were discussing Venous Gas Emboli detection techniques and consequences:
- i. Balestra et al (P-22) discussed the possible need for reducing ascent rates from diving, based on an analysis of dive profiles in the DAN Europe Diving Safety Laboratory (DSL) Database. Within a sample group of 105 recreational air diving profiles, matched for demographics and diving conditions, the conservatism settings of the Bühlmann ZHL16 algorithm did not differ significantly whereas there appeared to be a clear influence of the ascent speed on the probability of DCS (12.2m/min vs 9.1 m/min, p=0.0047). Unfortunately, the lack of physiological data in current databases significantly limits the potential conclusions, however, the trend is clear and merits further investigation.
 - ii. Evgenidis (P-33) detailed the electrochemical principles used in the electrical impedance spectroscopy measurements of endothelial dysfunction following dives; this innovative method shows good agreement with ultrasound-detected Flow Mediated Dilation changes after a dive.
 - iii. Papadopoulou (P-43) showed that the evolution of VGE post dive (as evaluated with frame-based bubble counting on 2D echocardiography) significantly differs between individuals even when they have undergone the same dive profile. In particular, in divers for whom significant circulating bubbles are visible, the peak score varies and is observed at earlier or later time post dive. The authors highlight the need for a continuous assessment rather than two or three measuring points for VGE measurements.

2. Conference Statistics

- a. The attendance of EUBS2015 was 233, with 129 being EUBS members. 103 abstracts were submitted of which 3 were rejected or withdrawn after peer review by the Scientific Committee. In all, 55 oral presentations and 45 poster presentations were held.
- b. The "Zetterström Award" for best poster was awarded to F. Tillmans, T. Noy, R. Lüddecke, I. Rohde, B. Lohrie, S. Klapa, S. Sebens, H. Werr, A. Koch, W. Kähler: *Increase in T-cells after hyperoxic exposure of healthy humans in vivo without relevant induction in apoptosis*
- c. The "Patrick Musimu Award" for best presentation (oral or poster) was given to Danilo Cialoni, Massimo Pieri, Giulia Giunchi, Alberto Maria Lanzone, Nicola Sponsiello, Alessandro Marroni: *Detection of venous gas emboli after repetitive breath hold dives in a Taravana case*
- d. The Conference is mostly financed by individual registration fees. However, the following organizations and companies have been solicited and have offered some form of financial or logistical support:
 - i. Merwede IHC Hytech
 - ii. Haux Life Support GmbH
 - iii. Maquet (Getinge Group)

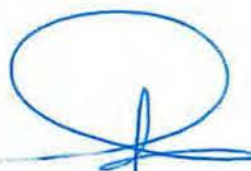
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 - IHC Merwede

e. The ONRG Grant has been used for

- i. Layout and printing of the Abstract and Conference Proceedings Book in hardcopy
- ii. Awards
- iii. Travel and/or accommodation for the following speakers
 - Hyper-Hypobaric Paradox Session
 - a. Paul Robach (ENSA, Genève, Switzerland)
 - b. Stéphane Tourreau (Annecy, France)
 - c. Francois Damilano (Chamonix, France)
 - Professional Diving Session
 - a. Theo Mavrostomos (Toulon, France)
 - b. Jean Lelièvre (EDTC & Hydrokarst, Grenoble, France)
 - c. Marc Borgnetta (INPP, Marseille, France)

- b. ONRG support was duly credited in the Abstract Book, with on-screen logo display during coffee and lunch breaks and by oral communication to the EUBS membership and beneficiaries.

Signed on behalf of the Grantee (EUBS):



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